Complete Summary

GUIDELINE TITLE

WHO recommendations for the prevention of postpartum haemorrhage.

BIBLIOGRAPHIC SOURCE(S)

World Health Organization (WHO). WHO recommendations for the prevention of postpartum haemorrhage. Geneva, Switzerland: World Health Organization (WHO); 2007. 116 p. [27 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Postpartum hemorrhage (PPH)

GUIDELINE CATEGORY

Prevention

CLINICAL SPECIALTY

Nursing
Obstetrics and Gynecology

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Hospitals
Nurses
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

To provide recommendations regarding the prevention of postpartum hemorrhage (PPH)

TARGET POPULATION

All women in labor

INTERVENTIONS AND PRACTICES CONSIDERED

1. Active management of the third stage of labor by skilled attendants to all women
2. Uterotonic drugs:
    - Oxytocin
    - Ergometrine/methylergometrine
    - Fixed drug combination of oxytocin and ergometrine
    - Misoprostol
    - Carboprost/sulprostone (considered, but not recommended)
3. Timing of cord clamping
4. Delivery of placenta by controlled traction

MAJOR OUTCOMES CONSIDERED

- Maternal mortality
- Maternal morbidity

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The search strategy aimed to identify systematic reviews and recent randomized trials for the prevention of postpartum haemorrhage (PPH).

For systematic reviews, the Cochrane Library (Issue 3, 2006) was searched for records with the following terms: "labour", "third stage", "active management",

"oxytocin", "ergometrine", "methylergometrine", "syntometrine", "misoprostol", "carboprost", "sulprostone", "uterotonics", "cord clamping", and "cord traction".

PubMed-Medline, Embase, Lilacs and IMEMR were also searched for records using the following terms: "labour OR labor", "third stage", "active management", "oxytocin", "ergometrine", "methylergometrine", "syntometrine", "misoprostol", "carboprost", "sulprostone", "uterotonics", "cord clamp*", "cord traction", "skilled providers", and "non-skilled providers"

Limits used were:

a. Type of studies
    - Randomized controlled trial
    - Meta-analysis
    - Reviews
b. Time limits

Whenever a systematic review from the Cochrane Library was identified, the publication year of the more recent study included in the systematic review was used as a time limit. No time limit was used when a systematic review from the Cochrane was not identified.

Draft summaries of the evidence were sent to the members of the Technical Consultation Group prior to the meeting and they were asked to identify any important evidence that had not been included.

NUMBER OF SOURCE DOCUMENTS

10 systematic reviews and 6 additional randomized trials

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

GRADE Quality Assessment Criteria

<table>
<tr><th>Quality of Evidence</th><th>Study Design</th><th>Lower If*</th><th>Higher If*</th></tr>
<tr><td>High</td><td>Randomized trial</td><td rowspan="4">Study Quality:

-1 Serious limitations

-2 Very serious</td><td rowspan="4">Strong Association:

+1 Strong, no plausible confounders, consistent and direct</td></tr>
<tr><td>Moderate</td><td></td></tr>
<tr><td>Low</td><td>Observational study</td></tr>
<tr><td>Very Low</td><td>Any other</td></tr>
</table>

Quality of Evidence	Study Design	Lower If*	Higher If*
	evidence	limitations -1 Important **inconsistency** **Directness**: -1 Some uncertainty -2 Major uncertainty -1 **Sparse data** -1 High probability of **Reporting Bias**	evidence** +2 Very strong, no major threats to validity and direct evidence*** +1 Evidence of a **Dose response** gradient +1 All **plausible confounders** would have reduced the effect

*1 = move up or down one grade (for example, from high to intermediate); 2 = move up or down two grades (for example, from high to low)

**A statistically significant relative risk of >2 (<0.5), based on consistent evidence from two or more observational studies, with no plausible confounders.

***A statistically significant relative risk of >5(<0.2) based on direct evidence with no major threats to validity.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Selection Criteria, Data Collection, and Judgements

Scoping questions and a list of beneficial and harmful outcomes of the intervention were sent by e-mail to an international panel of experts. Members of the panel were invited to comment on the relevance of the questions, to modify them if required, and to add additional relevant questions. Panel members were asked to rate each beneficial and harmful outcome on a scale of 1 to 9. A "critical outcome" was defined as an outcome that scored on average between 7 and 9. Those outcomes that scored between 4 and 6 on average were considered "important but not critical," while those scoring less than 4 were considered "not important."

Systematic reviews were used to summarize the evidence from randomized trials related to interventions for prevention of postpartum haemorrhage (PPH). Titles identified from the searches for reviews and assessed for the quality of relevant reviews were screened by two reviewers using checklists. For each question, data were extracted for all of the outcomes that were judged to be important, beginning with the most recent review of good quality and supplementing that with additional data from other good quality reviews that addressed the same question.

Evidence profiles were created using the GRADE approach. Using this approach, assessments of the quality of evidence for each important outcome take into account the study design, limitations of the studies, consistency of the evidence across studies, the directness of the evidence and the precision of the estimate. A liberal approach to assessment of study limitations was taken. Three main criteria were used for assessing trial limitations: concealment of allocation, blinding and follow-up. If most of the evidence for an outcome (based on the weight given to each study in the meta-analysis) came from trials that did not have serious limitations, the overall assessment for that outcome was that there were no important limitations.

If data were available as continuous outcomes, such as mean blood loss, absolute differences were presented as weighted mean difference (WMD). All estimates of effect size were expressed as relative risk if it was possible to calculate it from the data provided, with absolute risk estimates included where appropriate. In order to provide the panel with a broad and informative set of measures of effect, the numbers needed to treat (NNTs) and numbers needed to harm (NNHs) were calculated for each outcome. In systematic reviews, for each outcome, the lowest and highest baseline risks were extrapolated from control groups across the studies. The minimum and maximum NNTs and NNHs were therefore calculated, providing a range of values for these measures.

One reviewer extracted data from the reviews and prepared drafts of the evidence profiles with detailed footnotes explaining the judgements that were made. These were checked by at least one other member of the team and discussed with the team that prepared the background documentation.

All of the evidence profiles and additional tables were sent to the members of the Technical Consultation Group for review prior to the technical consultation.

Summary of Findings Tables

The key findings for each question were summarized in tables with the most important findings from the systematic reviews together with additional information from randomized clinical trials.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The World Health Organization (WHO) held a Technical Consultation on the Prevention of Postpartum Haemorrhage in Geneva on 18–20 October 2006 to discuss the various issues related to prevention of postpartum haemorrhage (PPH) and to develop recommendations.

Draft evidence tables prepared by Centro per la Valutazione della Effi cacia della Assistenza Sanitaria (Centre for the Evaluation of Effectiveness of Health Care) (CeVEAS) were reviewed by the WHO core team along with staff from CeVEAS. Evidence-based recommendations in response to the questions asked were then drafted.

See Tables 3 and 4 in Annex 4 of the original guideline document for more information about developing and grading recommendations.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strong recommendation: One for which the panel is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects.

Weak recommendation: One for which the panel concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, but the panel is not confident about these trade-offs.

See Annex 4 in the original guideline document for more information about grading the strength of recommendations.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

A draft of the methodology, results, and recommendations was sent for review to a sub-group of experts prior to their participation in the World Health Organization (WHO) Technical Consultation on Prevention of Postpartum Haemorrhage. The draft and the supporting evidence were reviewed at the Technical Consultation on Prevention or Postpartum Haemorrhage.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The rating schemes for the quality of the evidence (very low, low, moderate, high) and the strength of the recommendations (weak, strong) are defined at the end of the "Major Recommendations" field.

1. **Should active management of the third stage of labour be offered by skilled attendants for all women to prevent postpartum haemorrhage (PPH)? Should active management of the third stage be offered by non-skilled attendants to prevent PPH?**

   Recommendation

   - Active management of the third stage of labour should be offered by skilled attendants to all women. **(Strong recommendation, moderate quality evidence)**
     Recommendations on the individual components of active management are discussed below.
   - The panel does not recommend active management by non-skilled attendants.

   Remarks

   Although no evidence was found for or against the use of active management by non-skilled providers, the group placed high value on the potential risks – such as uterine inversion – that may result from inappropriate cord traction.

   ***Note**: Questions 2–6 are related to the selection of the uterotonic and summary tables, including evidence derived from trials comparing different uterotonics within the context of active management of the third stage of labour, assuming there is no interaction between the other components of active management and the uterotonic.*

2. **Should oxytocin (10 IU parenterally) or ergometrine/methylergometrine (0.25 mg parenterally) be offered to all women by skilled attendants to prevent PPH?**

   Recommendation

   In the context of active management of the third stage of labour, if all injectable uterotonic drugs are available:

   - Skilled attendants should offer oxytocin to all women for prevention of PPH in preference to ergometrine/methylergometrine. **(Strong recommendation, low quality evidence)**

   If oxytocin is not available:

   - Skilled attendants should offer ergometrine/methylergometrine or the fixed drug combination of oxytocin and ergometrine to women without hypertension or heart disease for prevention of PPH. **(Strong recommendation, low quality evidence)**

Remarks

These recommendations place a high value on avoiding adverse effects of ergometrine and assume similar benefit for oxytocin and ergometrine for preventing PPH.

3. **Should oral misoprostol (600 mcg) be offered to all women by skilled attendants to prevent PPH instead of oxytocin (10 IU intramuscular [IM])?**

Recommendation

In the context of active management of the third stage of labour:

- Skilled attendants should offer oxytocin for prevention of PPH in preference to oral misoprostol (600 mcg). **(Strong recommendation, high quality evidence)**

Remarks

This recommendation places a high value on the relative benefits of oxytocin in preventing blood loss compared to misoprostol, as well as the increased adverse effects of misoprostol compared to oxytocin.

4. **Should sublingual misoprostol (600 mcg) be offered to all women by skilled attendants to prevent PPH instead of oxytocin (10 IU IM)?**

Recommendation

In the context of active management of the third stage of labour:

- Skilled attendants should not offer sublingual misoprostol for prevention of PPH in preference to oxytocin. **(Strong recommendation, very low quality evidence)**
- Further research is needed to define the role of sublingual misoprostol administration for prevention of PPH.

5. **Should rectal misoprostol (600 mcg) be offered to all women by skilled attendants to prevent PPH instead of oxytocin (10 IU IM)?**

Recommendation

In the context of active management of the third stage of labour:

- Skilled attendants should not offer rectal misoprostol for prevention of PPH in preference to oxytocin. **(Strong recommendation, low quality evidence)**

Remarks

This recommendation places a high value on the known benefits of oxytocin and notes the significant uncertainty about whether rectal misoprostol is equivalent. Misoprostol has more adverse effects and a higher purchase cost.

6. **Should carboprost (0.25 mg)/sulprostone (0.5 mg) be offered to all women by skilled providers to prevent PPH instead of oxytocin (10 IU IM)?**

Recommendation

In the context of active management of the third stage of labour:

- Skilled attendants should not offer carboprost/sulprostone for prevention of PPH in preference to oxytocin. **(Strong recommendation, very low quality evidence)**

Remarks

This recommendation is based on the paucity of the evidence comparing the two treatments and the known effectiveness of oxytocin.

7. **In the absence of active management, should uterotonics be used alone for prevention of PPH?**

Recommendation

- In the absence of active management of the third stage of labour, a uterotonic drug (oxytocin or misoprostol) should be offered by a health worker trained in its use for prevention of PPH. (**Strong recommendation, moderate quality evidence**)

Remarks

For misoprostol, this recommendation places a high value on the potential benefits of avoiding PPH and ease of administration of an oral drug in settings where other care is not available, but notes there is only one study.

The only trial relevant to this recommendation used 600 mcg of misoprostol. The efficacy of lower doses has not been evaluated. There is still uncertainty about the lowest effective dose and optimal route of administration.

8. **When should the cord be clamped to maximize benefits for mother and baby?**

Recommendation

- Because of the benefits to the baby, the cord should not be clamped earlier than is necessary for applying cord traction in the active management of the third stage of labour. (**Weak recommendation, low quality evidence)**

- For the sake of clarity, it is estimated that this will normally take around 3 minutes.
- Early clamping may be required if the baby is asphyxiated and requires immediate resuscitation.

9. **Should the placenta be delivered by controlled traction in all women?**

   Recommendation

   Given the current evidence for active management includes cord traction, the panel does not recommend any change in the current practice. Further research is needed. **(Strong recommendation, very low quality evidence)**

Definitions:

GRADE Quality Assessment Criteria

Quality of Evidence	**Study Design**	**Lower If***	**Higher If***
High	Randomized trial	**Study Quality**: -1 Serious limitations -2 Very serious limitations -1 Important **inconsistency** **Directness**: -1 Some uncertainty -2 Major uncertainty -1 **Sparse data** -1 High probability of **Reporting Bias**	**Strong Association**: +1 Strong, no plausible confounders, consistent and direct evidence** +2 Very strong, no major threats to validity and direct evidence*** +1 Evidence of a **Dose response** gradient +1 All **plausible confounders** would have reduced the effect
Moderate			
Low	Observational study		
Very Low	Any other evidence		

*1 = move up or down one grade (for example, from high to intermediate); 2 = move up or down two grades (for example, from high to low)

**A statistically significant relative risk of >2 (<0.5), based on consistent evidence from two or more observational studies, with no plausible confounders.

***A statistically significant relative risk of >5(<0.2) based on direct evidence with no major threats to validity.

Strength of the Recommendations

Strong recommendation: One for which the panel is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects.

Weak recommendation: One for which the panel concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, but the panel is not confident about these trade-offs.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate management of the third stage of labor to prevent postpartum hemorrhage

POTENTIAL HARMS

Side effects of uterotonic drugs, including nausea, vomiting, diarrhea, high blood pressure, shivering, and temperatures over 38 degrees C

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QUALIFYING STATEMENTS

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IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The panel agreed that these recommendations should be disseminated and implemented through:

- Support from international professional organizations and partner agencies
- Working through regional and country offices (World Health Organization [WHO] and partners) for changes in policy and regulations
- Working towards including postpartum haemorrhage (PPH) prevention as an indication for use of misoprostol in the WHO essential medicines list
- Working on a press release and co-publication in several journals
- Translation into official languages one by one and disseminating recommendations in the available languages immediately
- Dissemination and implementation of the recommendations by professional associations, partner agencies, institutions and individuals
- Developing a feedback mechanism including obtaining information on dissemination and impact of the recommendations
- Developing a "PPH virtual network" to monitor evidence and develop a mechanism to determine appropriate time for update/development of new recommendations

IMPLEMENTATION TOOLS

Foreign Language Translations
Quick Reference Guides/Physician Guides
Staff Training/Competency Material

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

World Health Organization (WHO). WHO recommendations for the prevention of postpartum haemorrhage. Geneva, Switzerland: World Health Organization (WHO); 2007. 116 p. [27 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007

GUIDELINE DEVELOPER(S)

World Health Organization - International Agency

SOURCE(S) OF FUNDING

World Health Organization

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Authors: Matthews Mathai (Making Pregnancy Safer); A. Metin Gulmezoglu (Department of Reproductive Health and Research); Suzanne Hill (Department of Medicines Policy and Standards)

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All members of the expert panel declared their interests in writing prior to the meeting and orally at the start of the meeting. No potential conflict of interest was identified through this process.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the World Health Organization Web site.

Print copies: Available from the WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland; Phone: +41 22 791 3264; Fax: +41 22 791 4857; E-mail: bookorders@who.int.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Prevention of postpartum haemorrhage by active management of third stage of labour. MPS technical update. World Health Organization. 2006 Oct. 2 p. Electronic copies: Available from the World Health Organization Web site.
- Managing postpartum haemorrhage. Education materials for teachers of midwifery. 2nd edition. World Health Organization. 2006. 236 p. Electronic copies: Available in English and Portuguese from the World Health Organization Web site.
- Managing complications in pregnancy and childbirth: A guide for midwives and doctors. WHO, UNFPA, UNICEF, World Bank. 2000 Electronic copies: Available in English, French, Arabic, Indonesian, Italian, Russian, and Spanish from the World Health Organization Web site.
- Pregnancy, childbirth, postpartum and newborn care: A guide for essential practice. WHO, UNFPA, UNICEF, World Bank. 2000 Electronic copies: Available in English, French, Arabic, Portugese, and Russian from the World Health Organization Web site.

PATIENT RESOURCES

None available

NGC STATUS

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Date Modified: 3/9/2009